

Amendments To The Specification

Please delete and replace paragraph [0071] on pages 32-34 of the specification with the following replacement paragraph. Added matter relative to the previous version of the paragraph is indicated by underlining and bolding (since some of the original text was underlined when the application was filed):

[0071] The activity of the compounds according to this invention as inhibitors for the src-family tyrosine kinases was shown by using the following assay.

SRC-Inhibitor-Assay Parameters:

Reaction mixture:

ATP	5 μ M
Peptide (Ro + Ja133-Ro):	10 μ M
Ja133-Ro	196 nM
Ro	9.8 μ M
PT66	230 ng/ml

Assay buffer: 4 mM MgCl₂
 2 mM TCEP
 50 mM HEPES
 0,1 % Tween 20
 pH 7.3

Enzyme: 2.5 U/ml

Inhibitor: max. 25 μ M
 min. 0.42 nM

Material:

Eu-labelled phosphotyrosine antibody: - for Lck Cisbio Mab PT66-K,
 - for Src EG&G Wallac PT66 Eu-W1024
 (all commercially available).

Peptides: Ro: NH₂-A-E-E-E-I-Y-G-E-F-E-A-K-K-K-K-CONH₂ (SEQ ID NO: 1), and

Ja133-Ro: Ja133-G-Aminocaprylic acid-A-E-E-E-I-Y-G-E-F-E-A-K-K-K-K-CONH₂ (SEQ ID NO: 2), wherein Ja133 is LightCycler-Red 640-N-hydroxy succinimide ester ;

whereby both peptides were synthesized by an optimized solid phase peptide synthesis protocol (Merrifield, Fed. Proc. Fed. Amer. Soc. Exp. Biol. 21 (1962) 412) on a Zinsser SMP350 peptide synthesizer. Shortly, the peptide was assembled on 160 mg (22.8 µmol scale) of a Rink-Linker modified polystyrene solid phase by repeatedly conjugating an twenty fold excess of aminoacids each protected by temporary piperidine labile Fmoc- and permanent acid labile tert-Bu-, BOC- and Ottert-Bu-groups depending on the side chain function. The substrate sequence AEEEEYGEFEAKKKK (SEQ ID NO: 1) was N-terminal additionally mounted with the spacer amino acids Aminocaprylic acid and Glycin. After cleavage of the N-terminal temporary protecting group the still attached and protected peptide was labeled with a 1.5 fold amount of LightCycler-Red 640-N-hydroxy succinimide ester (purchased by Roche Diagnostics GmbH) and triethylamine. After 3 hrs. the resin was washed with Dimethylformamide and Isopropanol until the eluates of the blue resin got colorless. The fully protected and labeled peptide was removed from the solid phase and released from the permanent protecting groups by treatment with a mixture of 80% trifluoroacetic acid, 10% Ethanedithiol, 5% Thioanisole and 5% Water. The substrate was finally isolated by a preparative reverse phase HPLC purification. The purification yielded 12.2 mg RP-HPLC single peak pure blue material (lyophilisate). The identity was proven by MALDI mass spectroscopy [2720.0].

Enzymes: Upstate Lck (p56^{lck}, active), Upstate Src (p60^{c-src}, partially purified) were purchased from UBI.

Time-resolved Fluorescence Assay: Reader: Perkin Elmer, Wallac Victor 1420-040 multilabel counter; Liquid handling system: Beckman Coulter, Biomek 2000.

ATP, Tween 20, HEPES were purchased from Roche Molecular Biochemicals, MgCl_2 and MnCl_2 were purchased from Merck Eurolab, TCEP was purchased from Pierce, 384 Well low volume fluorescence plates was purchased from Falcon.

Assay Description: